

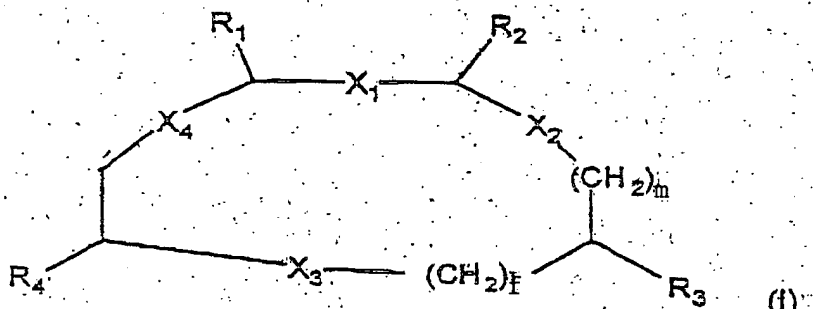
In response to the Office Action of November 26, 2002, please amend the application as follows:

In the Claims

Please amend claims 21-23, 25-27, 30 and 31, as follows:

--21. (Amended) Monocyclic compounds of formula (I)

wherein:



X_1 , X_2 , X_3 , X_4 are the same or different, and are selected from the group consisting of -CONR-, -NRCO-, -CH₂-NR-, and -NR-CH₂- where R is selected from the group consisting of H, C₁₋₃ alkyl, and benzyl;

f and m are the same or different, and is a number selected from the group consisting of 0, 1 and 2;

R_1 and R_2 , are the same or different, and represent:

-(CH₂)_rAr where r is 0, 1 or 2 and Ar is an aromatic group selected from the group consisting of benzene, naphthalene, thiophene, benzothiophene, pyridine, quinoline, indole, furan, benzofuran, thiazole, benzothiazole, imidazole, benzoimidazole, optionally substituted with up to 2 substituents selected from the group consisting of C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkyloxy,

C₂₋₄ amino-alkyloxy, halogens, OH, NH₂, CN, and NR₆R₇, where R₆ and R₇, same or different, are H or C₁₋₃ alkyl,

R₃ is-(CH₂)_rAr₁ where r is 0, 1 or 2 and Ar₁ is an aromatic group selected from the group consisting of benzene, naphthalene, thiophene, benzothiophene, pyridine, quinoline, indole, furan, benzofuran, thiazole, benzothiazole, imidazole, and benzimidazole,

C1 optionally substituted with up to 2 groups selected from the group consisting of C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkyloxy, amino-alkyloxy, halogens, OH, NH₂, and NR₆R₇, where R₆ and R₇, same or different, are H or C₁₋₃ alkyl,

R₄ is-NR₈R₉, where R₈ is H or C₁₋₃ alkyl; and

R₉ is selected from the group consisting of methanesulfonyl, tosyl, tetrahydropyranyl, tetrahydrothiopyranyl optionally mono or di-substituted by oxygen on the S atom, piperidyl, optionally substituted on the N-atom by a C₁₋₃ alkyl, C₁₋₃ acyl, aminosulfonyl, or methanesulfonyl; or a group-(CH₂)_gR₁₀ where g is 1,2, or 3 and R₁₀ is selected from the group consisting of morpholine, furan and CN;

or R₈ and R₉ together with the N atom to which they are linked form a piperazine optionally substituted at the other N atom substituted by a C₁₋₃ alkyl, C₁₋₃ acyl or methanesulfonyl;

-N(R₁₁)CO(CH₂)_hR₁₂ where R₁₁ is H or C₁₋₃ alkyl; h is 0, 1, 2 or 3; and R₁₂ is selected from the group consisting of morpholine, pyrrolidine optionally substituted with a hydroxy or hydroxymethyl, piperidine optionally substituted with a 4-hydroxy, 4-carboxyamido or 4-aminosulfonyl group, piperazine optionally substituted on the N-atom by C₁₋₃ alkyl, triazole, tetrazole, 5-mercapto-tetrazole, furan, thiophene, thiomorpholine, optionally mono or di-oxygenated on the S-atom, and amino- cyclohexane optionally substituted by a hydroxy group;

- COR₁₃ wherein R₁₃ is a member selected from the group consisting of morpholine and piperazine optionally substituted by a C₂₋₆ alkyl containing one or more hydroxy groups; their enantiomers and mixtures thereof, their diastereoisomers, and their pharmaceutically acceptable salts.

22. (Amended) Compound according to Claim 21 wherein:

f is 1

m is 0

X₁, X₂, X₃, X₄, are the same or different and are a member selected from the group consisting of -CONR- and -NRCO-,

where R is H or methyl,

R₁ and R₂ are the same or different, are:

-CH₂Ar wherein Ar is an aromatic group selected from the group consisting of benzene, pyridine, indole, optionally substituted with up to two substituents selected from the group consisting of C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkyloxy, C₂₋₄ amino alkyloxy, halogens, OH, NH₂, CN, and NR₆R₇, where R₆ and R₇, same or different, and are H or C₁₋₃ alkyl;

R₃ is -CH₂Ar₁ wherein Ar₁ is an aromatic group selected from the group consisting of alpha naphthyl, beta naphthyl, phenyl, phenyl substituted with up to two substituents selected from the group consisting of C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkyloxy, halogens, OH, and NH₂.

23. (Amended) Compounds according to Claim 22 wherein:

- X₁, X₂, X₃, X₄ are -CONH-,

- R₁ is indol-3-yl-methyl

- R₂ is phenyl-methyl optionally substituted with up to two substituents selected from the group consisting of chlorine, fluorine, CF₃, OH and CN, or are selected from the group consisting of 3-pyridyl-methyl and 4-pyridyl-methyl;

- R₃ is benzyl.

25. (Amended) Compounds according to Claim 24 represented by:

i) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}

ii) cyclo{Suc[1-(S)-(4-tetrahydropyranyl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}

iii) cyclo{Suc[1-(R)-(1-methyl-piperidin-4-yl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}

iv) cyclo{Suc[1-(R)-(4-tetrahydrothiopyranyl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}

v) cyclo{Suc[1-(R)-(1-oxo-tetrahydrothiopyran-4-yl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}

vi) cyclo{Suc[1-(R)-(1,1-dioxo-tetrahydrothiopyran-4-yl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}

vii) cyclo{Suc[1-(R)-N-methyl-N-(4-tetrahydropyranyl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}

viii) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Tyr-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}

ix) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Phe(4-F)-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}

- x) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Phe(3,5-F)-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
- xi) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Phe(4-CN)-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
- xii) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Phe(4-CF₃)-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
- C² xiii) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Ala(4-pyridyl)-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
- xiv) cyclo{Suc[1-(R)-(4-tetrahydropyranyl)amino]-Trp-Ala(3-pyridyl)-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
- xv) cyclo{Suc[1-(R)-(1-methylsulfonyl-piperidin-4-yl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
- xvi) cyclo{Suc[1-(R)-(1-aminosulfonyl-piperidin-4-yl)amino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
- xvii) cyclo{Suc[1-(R)-4-methyl-piperazin-1-yl]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
- xviii) cyclo{Suc[1-(R)-4-acetyl-piperazin-1-yl]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]} or
- xix) cyclo{Suc[1-(R)-4-methylsulfonyl-piperazin-1-yl]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}.

26. (Amended) Compounds according to Claim 23 wherein :

R_4 represents a group NR_8R_9 , where R_8 is H and R_9 is methanesulfonyl, tosyl or a group $-(CH_2)_gR_{10}$, wherein g is 1 or 2 and R_{10} is morpholine, furan, or CN.

27. (Amended) Compounds according to claim 26 represented by:

- C²
- xx) cyclo{Suc[1-(S)-methylsulfonylamino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
 - xxi) cyclo{Suc[1-(R)-methylsulfonylamino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
 - xxii) cyclo{Suc[1-(S)-(4-methylphenyl)sulfonylamino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
 - xxiii) cyclo{Suc[1-(R)-(4-methylphenyl)sulfonylamino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
 - xxiv) cyclo{Suc[1-(S)-2-(4-morpholino)ethylamino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
 - xxv) cyclo{Suc[1-(R)-2-(4-morpholino)ethylamino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}
 - xxvi) cyclo{Suc[1-(R)-(2-furyl)methylamino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]} or
 - xxvii) cyclo{Suc[1-(R)-cyanomethylamino]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}.
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30. (Amended) Compounds according to Claim 23 wherein:

R_4 represents a group COR_{13} wherein R_{13} is morpholine.

31. (Amended) Compounds according to claim 30 represented by:

- C³
- xlvi) cyclo{Suc[1-(4-morpholino)carbonyl]-Trp-Phe-[(R)-NH-CH(CH₂-C₆H₅)-CH₂NH]}.
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